rejected claims 1-18 for allegedly failing to (1) describe elements essential to the genus of atopic conditions and (2) indicate distinguishing attributes shared by members of the genera of nucleic acids having the generic formulae X_1CGX_2 or $X_1X_2CGX_3X_4$. For reasons set forth below, Applicants respectfully disagree and therefore request the Examiner to withdraw the rejection of claims 1-18 under 35 U.S.C. § 112, first paragraph, for alleged lack of adequate written description.

Applicants' representative thanks the Examiner for the opportunity to discuss this rejection in a telephone interview conducted July 29, 2003. As discussed in that interview, the specification provides dozens of examples of CpG nucleic acids having the generic formulae X_1CGX_2 or $X_1X_2CGX_3X_4$. Accordingly, Applicants' representative and the Examiner agreed in the telephone interview that the written description rejection would be withdrawn.

The Examiner also indicated that claims 1-18 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. The Examiner conceded that the specification is enabling for a method of modulating the immune response in mice and treating asthma in mice comprising the administration of CpG containing oligonucleotides comprising SEQ ID NO:10. However, the Examiner rejected claims 1-18 for allegedly lacking enablement for the ability to treat any and/or all atopic conditions in any organism comprising the administration of any CpG-containing oligonucleotide. For reasons set forth below, Applicants respectfully disagree and therefore request the Examiner to withdraw the rejection of claims 1-18 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement.

Applicants' representative thanks the Examiner for the opportunity to discuss this rejection in the same telephone interview conducted July 29, 2003. The Examiner agreed in the course of that interview that the rejection could be overcome if (a) the universe of atopic diseases is small, (b) atopic diseases share a common pathogenic mechanism affected by CpG nucleic acids, and (c) Applicants provide evidence of efficacy of the claimed method in at least one atopic condition in addition to asthma.

Atopic conditions are generally accepted to encompass a relatively discrete set of disorders which include allergic rhinitis (hay fever), allergic conjunctivitis, bronchial asthma,

atopic dermatitis (eczema, urticartia), and food allergies. Many of these are the very conditions disclosed in the specification at page 12, lines 30-32.

Atopic disorders are also generally believed to share a common IgE-mediated mechanism or pathogenesis. IgE is widely accepted to be a classic Th2-associated class of immunoglobulin. The specification teaches throughout that CpG nucleic acids can steer an immune response away from a Th2-like phenotype and toward a Th1-like phenotype. Thus the specification is enabling for methods of treating any atopic condition because the CpG nucleic acid used in the practice of the method inhibits IgE production. Given the relatively small number of atopic conditions and their mechanistic similarities, Applicants respectfully suggest the breadth of the claims is not unduly broad and the amount of experimentation is not unduly burdensome.

As further support for withdrawal of the rejection, Applicants offer evidence that the claimed method can be applied to atopic conditions in addition to asthma. This evidence includes two publications (Hussain I et al., Modulation of murine allergic rhinosinusitis by CpG oligodeoxynucleotides. *Laryngoscope*. 2002 Oct;112(10):1819-26; and Magone MT et al., Systemic or mucosal administration of immunostimulatory DNA inhibits early and late phases of murine allergic conjunctivitis. *Eur J Immunol*. 2000 Jul;30(7):1841-50) and a declaration under 37 C.F.R. § 1.132 by co-inventor Dr. Joel Kline describing unpublished data showing efficacy of CpG nucleic acids in a murine model of atopic dermatitis.

The Hussain reference specifically teaches that CpG ODN is useful in the treatment of allergic rhinitis in vivo. More specifically, the Hussain reference teaches that exposure to CpG ODN 1826 (TCCATGACGTTCCTGACGTT, corresponding to SEQ ID NO:10 of the specification) at the time of antigen sensitization significantly reduces nasal symptoms (scratching and sneezing) and eosinophilia (both submucosal upper airway and bone marrow) in mice upon challenge with aerosolized antigen.

The Magone reference specifically teaches that CpG ODN is useful in the treatment of allergic conjunctivitis in vivo. More specifically, the Magone reference teaches that systemic or mucosal administration of CpG ODN (TGACTGTGAACGTTCGAGATGA) after allergen (ragweed) sensitization inhibited both the immediate hypersensitivity response and the late-phase cellular infiltration and induced a ragweed-specific Th1 response in mice. Furthermore, CpG

ODN administration was shown to suppress the rise of ragweed-specific IgE titers after repeated allergen challenge.

The declaration of Dr. Joel Kline establishes CpG ODN is useful in the treatment of atopic dermatitis in vivo. More specifically, the declaration of Dr. Joel Kline shows that CpG ODN 1826 reduced skin eosinophilia in mice that are epicutaneously sensitized to antigen.

Applicants thus have provided evidence of efficacy of the claimed method in three atopic conditions in addition to asthma.

In view of the foregoing, Applicants submit that they have met the conditions established in the telephone interview with the Examiner to overcome the rejection based on alleged lack of enablement. Accordingly Applicants respectfully request that the Examiner withdraw the rejection of claims 1-18 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement.

Summary

Applicants have presented arguments and provided supportive evidence to overcome all rejections made by the Examiner. Applicants believe the claims are in condition for allowance. A prompt and favorable action is respectfully requested.

Respectfully submitted,

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